# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



| Applicant's or agent's file reference<br>SCB 871 PCT | **FOR FURTHER ACTION** | See Form PCT/IPEA/416 |
|---|---|---|
| International application No.<br>PCT/EP2004/008577 | International filing date *(day/month/year)*<br>30.07.2004 | Priority date *(day/month/year)*<br>08.08.2003 |
| International Patent Classification (IPC) or national classification and IPC<br>A61K47/38 | | |
| Applicant<br>MIPHARM S.P.A. | | |

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the opinion |
| ☐ | Box No. II | Priority |
| ☐ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☒ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☒ | Box No. VIII | Certain observations on the international application |

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 06.06.2005 | 22.11.2005 |
| Name and mailing address of the international preliminary examining authority:<br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized Officer<br>Vermeulen, S<br>Telephone No. +49 89 2399-7520 |

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/008577

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

| **Description, Pages** | |
|---|---|
| 1-8 | as originally filed |
| **Claims, Numbers** | |
| 1-4 | received on 08.06.2005 with letter of 06.06.2005 |
| **Drawings, Sheets** | |
| 1/4-4/4 | as originally filed |

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/008577

## Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-4 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-4 |
| Industrial applicability (IA) | Yes: | Claims | 1-4 |
| | No: | Claims | |

2. Citations and explanations (Rule 70.7):

**see separate sheet**

## Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

## Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Reference is made to the following documents:

   D1: WO 03/094920 A (DE BETHUNE MARIE-PIERRE T M M ; STOFFELS PAUL (BE); VAN ROEY JENS MARC) 20 November 2003
   D2: WO 01/28515 A (GIZURARSON SVEINBJORN ; SKULASON SKULI (IS); HOLBROOK W PETER (IS); KR) 26 April 2001
   D3: JONES DAVID S ET AL., INTERNATIONAL JOURNAL OF PHARMACEUTICS (AMSTERDAM), vol. 151, no. 2, 1997, pages 223-233
   D4: CARLAN S J ET AL., OBSTETRICS AND GYNECOLOGY, vol. 90, no. 6, December 1997 (1997-12), pages 911-915
   D5: SYED TANWEER A ET AL., INTERNATIONAL JOURNAL OF STD AND AIDS, vol. 11, no. 6, June 2000 (2000-06), pages 371-374
   D6: BIRNIE CHRISTINE R ET AL., JOURNAL OF PHARMACEUTICAL SCIENCES, vol. 90, no. 9, September 2001 (2001-09), pages 1386-1394
   D7: BALLAGH S A ET AL., CONTRACEPTION, vol. 66, no. 5, November 2002 (2002-11), pages 369-375
   D8: US 2003/0039704 A (ARKIN ET AL) 27 February 2003 (2003-02-27)
   D9: US 5,849,761 B (YAKSH) 15 December 1998 (1998-12-15)

   The documents D8 and D9 were not cited in the international search report. Copies of the documents are appended hereto.

2. The subject-matter of claims 1-4 is considered novel because it is not directly and unambiguously disclosed in the cited state of the art (Article 33(2) PCT).

3. The subject-matter of claims 1-4 does not involve an inventive step (Art. 33(3) PCT) because having regard to the cited prior art it is obvious to a person skilled in the art (Article 33(3) PCT).

3.1 Hydrogels based on hydroxyethylcellulose as the only gelling and bioadhesive agent are disclosed e.g. in D4, D5 and D7. The gels disclosed therein are used for delivery of an active agent through vaginal mucosae. For example, D5 discloses effective delivery of 5-fluorouracil. Although said documents do not explicitly study the bioadhesive capacity of the disclosed hydrogels, a certain level of bioadhesion is implicitly presence, only due to the fact that the disclosed hydrogels are based on hydroxyethylcellulose. It should be noted that hydroxyethylcellulose is generally known to produce bioadhesive hydrogels. Reference is made to e.g. D3, which studies the bioadhesive properties of aqueous hydroxyethylcellulose gels.

3.2 The hydroxyethylcellulose based hydrogels disclosed in the above mentioned documents differ from the presently claimed hydrogel only by the presence in the latter of further additives such as glycerol, diethylene glycol monoethyl ether, surfactants, preservatives and acidifiers. However, the addition of such additives, although not explicitly disclosed in D3, D4, D5 and D7, falls within standard formulation practice which is considered obvious to a the skilled person. More particularly, the claimed additives are very common ingredients in the formulation of topical compositions for delivery of active agents to the skin or mucosal tissues. For example, glycerol and diethylene glycol monoethyl ether are common penetration enhancers. Hydroxyethylcellulose based hydrogels comprising one or more of such additives are known e.g. from D8 (cf. examples 1-4) and D9 (examples 5-6).

4. The subject-matter of claims 1-4 is considered to be industrially applicable and accordingly meets the requirements of Art.33(4) PCT.

**Re Item VI**
**Certain documents cited**

Document D1, published after the effective date of filing of the present application, contains subject-matter (cf. passages cited in the ISR) which may be relevant to the present application (Rule 70.10 PCT).

**Re Item VIII**

**Certain observations on the international application**

The examples of the invention described on pages 3 and 4 do not fall within the scope of the independent claim. This inconsistency between the claims and the description leads to doubt concerning the matter for which protection is sought, thereby rendering the claims unclear, Article 6 PCT.

## CLAIMS

1. Compositions in the form of an aqueous bioadhesive gel for the delivery of active ingredients and/or principles, comprising hydroxyethylcellulose as the only gelling and bioadhesive agent.

~~2. Compositions in the form of an aqueous gel, as claimed in claim 1, for the intravaginal delivery of active ingredients and/or principles.~~

~~3. Compositions as claimed in claim 1 or 2, further containing~~ glycerol, diethylene glycol monoethyl ether, surfactants, preservatives and acidifiers.

2. ~~4.~~ Compositions as claimed in claim 1, ~~3~~, containing 1 to 5% by weight of hydroxyethylcellulose, 25 to 90% by weight of water, 5 to 25% by weight of glycerol, 5 to 50% by weight of diethylene glycol monoethyl ether, 0.01 to 10% by weight of surfactants, 0.05 to 1% by weight of preservatives, and 0.01 to 1% by weight of acidifiers.

3. ~~5.~~ Compositions as claimed in any of claims 1 to 2, ~~4~~, containing as active constituents antifungals, antiseptics and antimicrobials, antibiotics, analgesics, local anaesthetics, antihistamines, anti-inflammatory agents, contraceptives, hormones, or combinations thereof.

4. ~~6.~~ Compositions as claimed in claim 3, ~~5~~, wherein the active ingredient is selected from econazole, miconazole, fluconazole, cyclopiroxolamine, nifuratel, nystatin, chlorhexidine, ibuprofen, ketoprofen, naproxen, benzydamine, benzalkonium chloride or other quaternary ammonium antiseptics, and nonoxynol-9.